

consists essentially of a glycosylated polypeptide having an apparent relative molecular mass  $M_r$  of about 43 kDa as determined by its electrophoretic mobility when subjected to 15% SDS-PAGE electrophoresis and having homology in amino acid sequence with the amino acid sequence (SEQ ID No: 1) of human plasma Zn- $\alpha_2$ -glycoprotein.

- 33. (New) A lipid mobilizing agent as claimed in claim 32 which is obtainable by a process that includes sequential steps of subjecting biological material to ion exchange chromatography, exclusion chromatography, and then to hydrophobic interaction chromatography, said biological material being urine from a cancer cachexia patient or an extract of a culture of a MAC16 tumor cell line deposited under the provisions of the Budapest Treaty in the European Collection of Animal Cell Cultures (ECACC) under an Accession No. 89030816.
- 34. (New) A biologically active lipid mobilizing agent as claimed in claim 31 for therapeutic use which is a glycosylated polypeptide wherein the polypeptide moiety is selected from one of the following groups:
  - (a) a polypeptide having the amino acid sequence of a Zn-α<sub>2</sub>-glycoprotein;
  - (b) a polypeptide which in respect to (a) is deficient in one or more amino acids that do not significantly affect the lipid mobilizing the lipolytic activity;



- (c) a polypeptide in which in respect to (a) one or more amino acids are replaced by a different amino acid or acids that do not significantly affect the lipid mobilizing or lipolytic activity;
- (d) a polypeptide in which in respect to (a) there is incorporated a plurality of additional amino acids which do not interfere with the biological lipolytic activity.
- 35. (New) A biologically active lipid mobilizing agent for use in therapy as claimed in claim 31 consisting essentially of a glycoprotein that has a polypeptide amino acid sequence homologous with the amino acid sequence (SEQ ID No: 1) of human plasma Zn- $\alpha_2$ -glycoprotein, or with a variant thereof which is modified by minor additions, deletions, or substitutions that do not substantially affect its lipid mobilizing activity in biological systems.
- 36. (New) A lipid mobilizing agent for use in therapy as claimed in claim 34 or 35 further characterized in that it has an apparent relative molecular mass M<sub>r</sub> of about 43 kDa as determined by its electrophoretic mobility when subjected to 15% SDS-PAGE electrophoresis.
- 37. (New) A lipid mobilizing agent for use in therapy as claimed in claim 31 wherein its lipid mobilizing properties are destroyed when subjected to digestion with chymotrypsin.



- 38. (New) A lipid mobilizing agent for use in therapy as claimed in claim 31 wherein it has the potential *in vitro* to stimulate adenylate cyclase activity in a guanine triphosphate (GTP) dependent process upon incubation with murine dipocyte plasma membranes.
- 39. (New) A lipid mobilizing agent for use in therapy as claimed in claim 31 which has substantially the same immunological properties as human Zn- $\alpha_2$ -glycoprotein.
- 40. (New) A biologically active lipid mobilizing agent for use in therapy which is capable of inducing lipolysis in marnmalian adipocytes characterized, which has an apparent molecular mass M<sub>r</sub> as determined by gel exclusion chromatograph greater than 6.0 kDa, and which is obtainable by subjecting the lipid mobilizing agent claimed in claim 31 to fragmentation by enzymatic degradation.
- 41. (New) A biologically active lipid mobilizing agent as claimed in claim 40 for use in therapy that is a fragment of a glycoprotein or glycosylated polypeptide which is a component of the lipid mobilizing agent claimed in claim 31 produced by digesting the latter with trypsin.
- 42. (New) A lipid mobilizing agent for use in therapy as claimed in claim 31 which is substantially free of proteolytic activity.

Gut B1

- 43. (New) A lipid mobilizing agent for use in therapy as claimed in claim 31 wherein the polypeptide chain of the polypeptide component has an N-terminus blocked by a pyroglutamate residue.
- 44. (New) A lipid mobilizing agent for use in therapy as claimed in claim 31 wherein the lipid mobilizing activity is destroyed by periodate treatment.
- 45. (New) A method of isolating and purifying a lipid mobilizing agent having the properties and characteristics of a Zn-α<sub>2</sub>-glycoprotein, said method comprising subjecting an extract of a cachexia-inducing tumor or of a culture of a cachexia-inducing tumor cell line, or a sample of urine or other body fluid of a mammal bearing a cachexia-inducing tumor, to a combination of ion exchange, gel filtration size exclusion chromatography, and hydrophobic interaction chromatography, and recovering a single product or molecular species having an apparent relative molecular mass of 43 kDa, as determined by 15% SDS-PAGE electrophoresis, which is substantially free of proteolytic activity.
- 46. (New) A pharmaceutical composition for use in treating mammals, said composition containing as the active constituent an effective therapeutic amount of a lipid mobilizing agent as claimed in claim 31, together with a pharmaceutically acceptable carrier, diluent or excipient.

- 47. (New) A pharmaceutical composition as claimed in claim 46 which is an injectable formulation incorporating a carrier in the form of a pharmaceutically acceptable injection vehicle.
- 48. (New) A method of treating a mammal to bring about a weight reduction or reduction in obesity, said method comprising administering to the mammal in need of such treatment a therapeutically effective dosage of a lipid mobilizing agent as claimed in claim 31.
- 49. (New) A method of treating a mammal to bring about a weight reduction or reduction in obesity, said method comprising administering to the mammal in need of such treatment a therapeutically effective dosage of a glycoprotein identical to or homologous with human Zn-α<sub>2</sub>-glycoprotein, or an effective lipolytically active fragment thereof which has an apparent molecular mass M<sub>r</sub> as determined by gel exclusion chromatography that is greater than 6.0 kDa, substantially free of any proteolytic agrivity.
- 50. (New) A diagnostic method for detecting the presence of a tumor in a mammal and/or for monitoring the progress of treatment of such a tumor, said method comprising taking from said mammal a sample of urine, blood serum or other body fluid and testing to detect the presence of and/or to measure the amount therein of Zn-a<sub>2</sub>-glycoprotein.

Cnt B1

- 51. (New) A diagnostic method as claimed in claim 50 wherein the testing is carried out by use of a biochemical reagent capable of specifically recognizing and binding to  $Zn-\alpha_2$ -glycoprotein.
- 52. (New) A diagnostic method as claimed in claim 51 wherein the biochemical reagent is a monoclonal or polyclonal antibody.
- 53. (New) A diagnostic method as claimed in claim 50 which is applied to a sample of urine.
- 54. (New) A diagnostic kit for carrying out the method of claim 50, said kit comprising a receptacle for receiving the sample of body fluid, a biochemical reagent for detecting Zn-α<sub>2</sub>-glycoprotein, and instructions for use of said kit.
- 55. (New) Use of a lipid mobilizing agent as defined in claim\_31 for producing antibodies for use as a diagnostic detecting agent for use in therapy as inhibitors or antagonists to the lipid mobilizing agent causing cachexia in cancer patients.
- 56. (New) Use of a preparation of antibodies for the manufacture of a medical preparation or medicament for the treatment of cachexia-associated cancer and/or tumors, wherein said antibodies are capable of specifically recognizing and binding to the lipid mobilizing agent claimed in claim 31.



- 57. (New) Use as claimed in claim 56 of a preparation of antibodies wherein the antibodies are monoclonal antibodies.
- 58. (New) Use of a lipid mobilizing agent as defined in claim 31 for screening and identifying and/or for carrying out investigations of possible lipolytic activity inhibiting agents having potential as anti-cachectic or anti-tumor therapeutic agents.
- 59. (New) Use as claimed in-claim 58 wherein samples of possible antagonists to, or inhibitors of, the activity of said lipid mobilizing agent are added to preparations of said lipid mobilizing agent, followed by incubation *in vitro* with a preparation of adipocytes and assaying to determine the level of lipolytic activity relative to that of a control sample.